Docket No. CRD0850 USNP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Gregory A. Kopia et al.	Art Unit: 3743
Serial No.	:	09/575,480	Confirmation No. 1106
Filed	:	May 19, 2000	Examiner: C.T. Nguyen
For	:	DRUG COMBINATIONS USEFUL FOR PREVENTION OF RESTENOSIS	

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June 28, 2007	Paul A. Coletti
Date of Transmission and Signature	**Name of Applicant, Assignee, or Registered Representative**

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Signature

Commissioner for Patents
P.O. Box 1450
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RESPONSE UNDER MPEP § 1205.03

Dear Sir:

In response to the Notice dated June 4, 2007, Applicants respond under MPEP § 1205.03 as follows, by filing this substitute "Summary of Claimed Subject Matter":

Summary of Claimed Subject Matter

The invention embodied by the subject application on appeal is directed to an approach to solving the clinical problem of restenosis, which involves the administration of drug combinations, either locally or systemically. One example of such a combination would be the addition of the anti-inflammatory corticosteroid, dexamethasone, with an antiproliferative agent such as rapamycin or its analogues. Delivery of a stent containing both an ***antiproliferative agent and an anti-***

inflammatory agent (emphasis added) to a coronary artery injured during the process of angioplasty would provide the added therapeutic benefit of:

1. Limiting the degree of local smooth muscle cell proliferation;
2. Reducing a stimulus for proliferation, i.e., inflammation, and thus enhance the restenosis-limiting action of the stent.

An additional benefit of combination drug therapy may be to reduce the dose of each of the therapeutic components and thus limiting their toxicity, while still achieving a reduction in restenosis. See Table 1 (included below), which demonstrates that concentrations of rapamycin or dexamethasone below their respective IC_{50} amounts may combine to produce an effect on cell growth greater than either agent individually.

% of Control Growth	**Concentration of Dexamethasone**									
	0	0.01	0.05	0.1	0.5	1.0	5.0	10	50	100
Rapamycin 0 ug/ml	100.0	-	-	75.2	76.5	72.2	50.0	36.1	18.3	11.7
Standard Deviation	4.2			0.8	16.3	9.3	7.6	5.9	6.0	1.3
Rapamycin 0.2 ug/ml	85.7	63.4	57.6	49.7	48.9	48.2	41.2	31.1	31.2	29.0
Standard Deviation	6.6	3.2	2.1	4.6	2.2	1.7	3.0	2.7	1.0	1.8
Rapamycin 1.0 ug/ml	67.4	48.3	45.1	38.1	39.2	37.8	33.9	25.8	20.7	18.5
Standard Deviation	2.6	3.3	13.3	9.5	4.4	4.5	3.1	8.1	6.4	3.7

Table 1: Inhibition of human vascular smooth muscle cell proliferation with dexamethasone or dexamethasone + rapamycin.

Further aspects of this summary are seen in the specification at page 8, lines 7-23, page 10, lines 14-28, page 11, lines 11-15, and page 13, lines 11-20.

According to the claims, Claim 1 (the sole remaining independent claim) provides:

1. A method for treating restenosis comprising an intravascular infusion or delivery by release from a surface of a stent of a combination of at least two agents, including an anti-proliferative agent for inhibiting smooth muscle cell growth comprising rapamycin or an analogue

thereof and an anti-inflammatory agent for inhibiting smooth muscle growth, both said agents contained in therapeutic dosage amounts.

So, treatment of restenosis is discussed at, for instance, page 2, line 11 to page 6, line 29. The treatment of restenosis via stents is discussed at page 7, lines 5-12. The treatment of restenosis via a stent coated with an antiproliferative and an anti-inflammatory agent coated on a stent is discussed at page 8, lines 17-24, and page 11, lines 17-27. Moreover, coated stents are disclosed in the stents of Figures 1-4. At least example 1 discusses the use of the antiproliferative agent rapamycin. This discussion can be read at page 12, line 20 to page 15, line 6. Other examples occur throughout the disclosure.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Account No. 10-0750/CRD-850USNP/PAC.

Respectfully submitted,

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